Attorney Docket No. UAB-16152/22

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: UAB Research Foundation

Int'l Application No.: PCT/US00/40165

Filed: 08 June 2000

Title: HERPES SIMPLEX VIRUS EXPRESSING FOREIGN GENES AND METHOD FOR TREATING CANCERS THEREWITH

STATEMENT

Assistant Commissioner for Patents
Attn: Box PCT
Washington, D.C. 20231

Dear Sir:

Applicant submits that the amendments being made are to further clarify the case and the appended claims.

It is desired to note that the claimed subject matter is novel and can be shown to comprise an inventive step, evidence of which Applicants reserve the right to make of record in due course of the prosecution.

The above amendment does not go beyond the disclosure in the international application as filed.

Respectfully submitted,

Ellen A. Cogen

Ellen S. Cogen, Reg. No. 38,109
Gifford, Krass, Groh, Sprinkle,
Anderson & Citkowski, P.C.
280 N. Old Woodward Ave., Suite 400
Birmingham, MI 48009-5394
(248) 647-6000

Dated: December 10, 2001

Attorney Docket No. UAB-16152/22

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: UAB Research Foundation

Int'l Application No.: PCT/US00/40165

Filed: 08 June 2000

Title: HERPES SIMPLEX VIRUS EXPRESSING FOREIGN GENES AND METHOD FOR TREATING CANCERS THEREWITH

AMENDMENT UNDER RULES 66.3 AND 66.8

Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231

Sir:

Pages 25-26 are being submitted containing claims 1-15. The status of these claims are as follows:

Claim 1 has been amended for clarity and to clearly define over the art of record.

Claim 9 has been amended to clearly define over the art of record.

The remaining claims are unchanged.

Claims 1-15 were held to lack novelty under PCT Article 33(2) as being anticipated by Toda, et al. Toda, et al. is cited as teaching intratumoral administration of a replication competent HSV encoding IL-12 wherein the HSV comprises a deletion in the $\gamma_1$34.5 gene. Toda, et al. are further cited as teaching antitumoral activity wherein the cancer vaccine comprising the HSV comprising a deletion in the $\gamma_1$34.5 gene further comprises a heterodimeric cytokine IL-12, comprising 35kDa (p35) and 40kDa (p40) subunits.

Claim 1 includes a step of "administering to a subject a therapeutically effective amount of a herpes simplex virus (HSV) comprising a nucleic acid sequence encoding an agent ... such that a direct anti-cancer response is induced in the subject." (claim 1, lines 3-7) A method of claim 1 of the present invention includes administration of a vector having a "primary characteristic of direct tumor cell oncolysis..." (p.5, line 4) In contrast, Toda, et al. describe an indirect method of affecting cancer cells, using herpes simplex virus (HSV) comprising a nucleic acid sequence encoding IL-12 as an "in situ cancer vaccine" that "... induces a tumor-specific immune response ..." (Toda, et al., p. 4457, 2nd column, lines 12-14). Since the vaccination method of Toda, et al. necessarily involves cells other than the tumor cells, specifically immune cells, in an anti-cancer treatment, it is by definition indirect. The method of the present invention, in contrast, directly affects tumor cells to effect treatment. On the basis of the amendment and these arguments, it is submitted that independent claim 1 is novel over Toda, et al. under PCT Article 33(2). Likewise, it is submitted that claims 2-8 which depend therefrom are not anticipated by Toda, et al.

Claim 9 includes a "nucleic acid sequence encoding for ... IL-12, ...operatively linked to a mammalian promoter..." (claim 9, lines 2-4) In contrast, Toda, et al. describe a herpes simplex virus comprising a nucleic acid sequence "... with the CMV promoter driving IL-12." (Toda, et al., p. 4457, 2nd column, lines 24-25) Toda et al. further describe the viral promoter as preferred since "... expression is strong but transient." (Toda, et al., p. 4457, 2nd column, lines 24-25) On the basis of the amendment and these arguments, it is submitted that independent claim 9 is novel over Toda, et al. under PCT Article 33(2). Likewise, it is submitted that claims 10-15 which depend therefrom are not anticipated by Toda, et al.

It is now believed that all the claims define novelty and inventive step over the prior art. If the Examiner finds to the contrary, it is respectfully requested that the undersigned in

charge of this application be called at the telephone number given below in order to resolve any remaining issues.

Respectfully submitted,

Ellen A. Cogen

Ellen S. Cogen, Reg. No. 38,109
Gifford, Krass, Groh, Sprinkle,
Anderson & Citkowski, P.C.
280 N. Old Woodward Ave., Suite 400
Birmingham, MI 48009-5394
(248) 647-6000

Dated: October 1, 2001

GS–W:\Word Processing\Jks\UAB16152-amd.doc